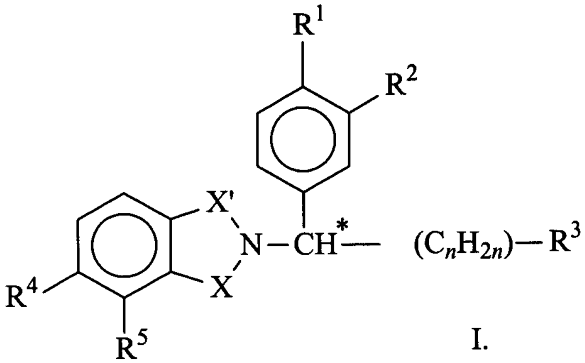
What is claimed is:

1. A method of reducing elevated levels of PDE IV in a mammal which comprises administering thereto an effective amount of a substantially chirally pure (R)-compound, a substantially chirally pure (S)-compound, or a mixture of (R)- and (S)-compounds selected from the group consisting of

(a) compounds having the formula (I):



I.

wherein:

each of R^1 and R^2, independently of the other, is selected from the group consisting of alkyl of 1 to 4 carbon atoms, alkoxy of 1 to 4 carbon atoms, cyano, cycloalkoxy of 3 to 18 carbon atoms, cycloalkyl of 3 to 18 carbon atoms, and cycloalkylmethoxy in which cycloalkyl has from 3 to 18 carbon atoms;

one of X and X' is =C=O and the other of X and X' is =C=O or $=CH_2$;

R^3 is selected from $-SO_2-Y$, -COZ, -CN, and hydroxyalkyl of 1 to 6 carbon atoms in which

Y is selected from alkyl of 1 to 6 carbon atoms, phenyl, and benzyl;

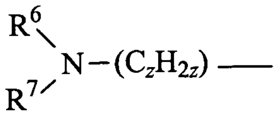
Z is selected from $-NR^{6''}R^{7''}$, alkyl of 1 to 6 carbon atoms, phenyl, and benzyl;

$R^{6''}$ is selected from hydrogen, alkyl of 1 to 4 carbon atoms, cycloalkyl of 3 to 18 carbon atoms; phenyl, benzyl, and alkanoyl of 2 to 5 carbon atoms, each of which is unsubstituted or substituted with halo, amino, or alkylamino of 1 to 4 carbon atoms;

$R^{7''}$ is alkyl of 1 to 4 carbon atoms;

n has a value of 1, 2, or 3;

one of R^4 and R^5 is hydrogen and the other of R^4 and R^5 is, imidazolyl, pyrrolyl, oxadiazolyl, triazolyl, or



$$\begin{matrix} R^6 \\ \end{matrix}\!\!\searrow N-(C_zH_{2z})\text{——}\quad R^7\!\nearrow$$

in which *z* is 0 or 1;

R^6 when taken independently of R^7, is selected from cycloalkanoyl of 2 to 6 carbon atoms each of which is unsubstituted or substituted with halo, amino, monoalkylamino or dialkylamino in which each alkyl group contains 1 to 4 carbon atoms; and

R^7 is selected from hydrogen, alkyl of 1 to 4 carbon atoms, methylsufonyl, and alkoxyalkylcarbonyl of 2 to 5 carbon atoms; or,

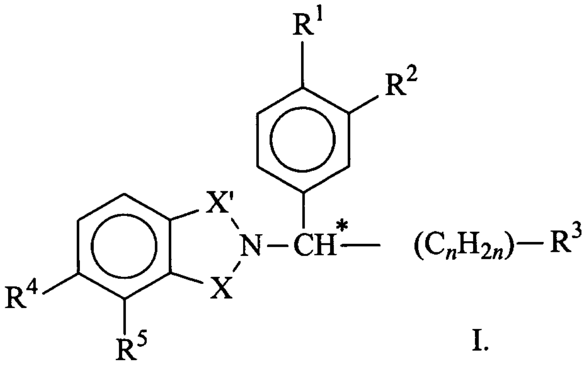
R^6 and R^7 taken together are alkylidene of 1 or 2 carbon atoms substituted by amino, alkylamino, or dialkylamino in which each alkyl group has from 1 to 4 carbon atoms or, provided z is 1, -CH=CH-CH=CH-, -CH=CH-N=CH-; and,

the carbon atom designated * constitutes a center of chirality; and

(b) an acid addition salt of any one of said compounds having the formula (I) which contains a nitrogen atom susceptible of protonation.

2. A method of reducing elevated levels of TNFα in a mammal which comprises administering thereto an effective amount of a substantially chirally pure (R)-compound, a substantially chirally pure (S)-compound, or a mixture of (R)- and (S)-compounds selected from the group consisting of

(a) compounds having the formula (I):



I.

wherein:

each of R^1 and R^2, independently of the other, is selected from the group consisting of alkyl of 1 to 4 carbon atoms, alkoxy of 1 to 4 carbon atoms, cyano, cycloalkoxy of 3 to 18 carbon atoms, cycloalkyl of 3 to 18 carbon atoms, and cycloalkylmethoxy in which cycloalkyl has from 3 to 18 carbon atoms;

one of X and X' is =C=O and the other of X and X' is =C=O or $=CH_2$;

R^3 is selected from $-SO_2-Y$, -COZ, -CN, and hydroxyalkyl of 1 to 6 carbon atoms in which

Y is selected from alkyl of 1 to 6 carbon atoms, phenyl, and benzyl;

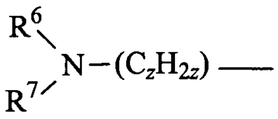
Z is selected from $-NR^{6''}R^{7''}$, alkyl of 1 to 6 carbon atoms, phenyl, and benzyl;

$R^{6''}$ is selected from hydrogen, alkyl of 1 to 4 carbon atoms, cycloalkyl of 3 to 18 carbon atoms; phenyl, benzyl, and alkanoyl of 2 to 5 carbon atoms, each of which is unsubstituted or substituted with halo, amino, or alkylamino of 1 to 4 carbon atoms;

$R^{7''}$ is alkyl of 1 to 4 carbon atoms;

n has a value of 1, 2, or 3;

one of R^4 and R^5 is hydrogen and the other of R^4 and R^5 is, imidazolyl, pyrrolyl, oxadiazolyl, triazolyl, or



$$R^6R^7N-(C_zH_{2z})-$$

in which *z* is 0 or 1;

R^6 when taken independently of R^7, is selected from cycloalkanoyl of 2 to 6 carbon atoms each of which is unsubstituted or substituted with halo, amino, monoalkylamino or dialkylamino in which each alkyl group contains 1 to 4 carbon atoms; and

R^7 is selected from hydrogen, alkyl of 1 to 4 carbon atoms, methylsufonyl, and alkoxyalkylcarbonyl of 2 to 5 carbon atoms; or,

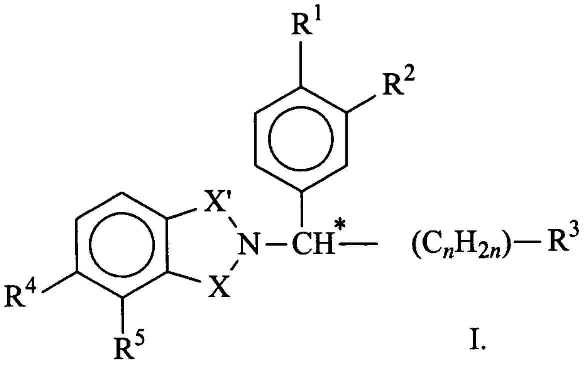
R^6 and R^7 taken together are alkylidene of 1 or 2 carbon atoms substituted by amino, alkylamino, or dialkylamino in which each alkyl group has from 1 to 4 carbon atoms or, provided z is 1, -CH=CH-CH=CH-, -CH=CH-N=CH-; and,

the carbon atom designated * constitutes a center of chirality; and

(b) an acid addition salt of any one of said compounds having the formula (I) which contains a nitrogen atom susceptible of protonation.

3. A method of reducing elevated levels of matrix metalloproteinase in a mammal which comprises administering thereto an effective amount of a substantially chirally pure (R)-compound, a substantially chirally pure (S)-compound, or a mixture of (R)- and (S)- compounds selected from the group consisting of

(a) compounds having the formula (I):


I.

wherein:

each of R^1 and R^2, independently of the other, is selected from the group consisting of alkyl of 1 to 4 carbon atoms, alkoxy of 1 to 4 carbon atoms, cyano, cycloalkoxy of 3 to 18 carbon atoms, cycloalkyl of 3 to 18 carbon atoms, and cycloalkylmethoxy in which cycloalkyl has from 3 to 18 carbon atoms;

one of X and X' is =C=O and the other of X and X' is =C=O or $=CH_2$;

R^3 is selected from $-SO_2-Y$, -COZ, -CN, and hydroxyalkyl of 1 to 6 carbon atoms in which

Y is selected from alkyl of 1 to 6 carbon atoms, phenyl, and benzyl;

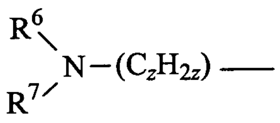
Z is selected from $-NR^{6'''}R^{7'''}$, alkyl of 1 to 6 carbon atoms, phenyl, and benzyl;

$R^{6'''}$ is selected from hydrogen, alkyl of 1 to 4 carbon atoms, cycloalkyl of 3 to 18 carbon atoms; phenyl, benzyl, and alkanoyl of 2 to 5 carbon atoms, each of which is unsubstituted or substituted with halo, amino, or alkylamino of 1 to 4 carbon atoms;

$R^{7'''}$ is alkyl of 1 to 4 carbon atoms;

n has a value of 1, 2, or 3;

one of R^4 and R^5 is hydrogen and the other of R^4 and R^5 is, imidazolyl, pyrrolyl, oxadiazolyl, triazolyl, or



$$R^6R^7N-(C_zH_{2z})-$$

in which *z* is 0 or 1;

R^6 when taken independently of R^7, is selected from cycloalkanoyl of 2 to 6 carbon atoms each of which is unsubstituted or substituted with halo, amino, monoalkylamino or dialkylamino in which each alkyl group contains 1 to 4 carbon atoms; and

R^7 is selected from hydrogen, alkyl of 1 to 4 carbon atoms, methylsufonyl, and alkoxyalkylcarbonyl of 2 to 5 carbon atoms; or,

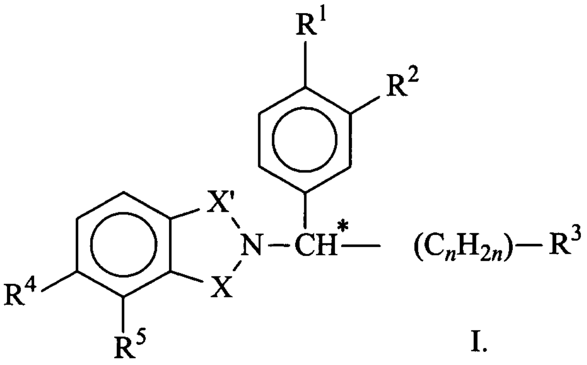
R^6 and R^7 taken together are alkylidene of 1 or 2 carbon atoms substituted by amino, alkylamino, or dialkylamino in which each alkyl group has from 1 to 4 carbon atoms or, provided z is 1, -CH=CH-CH=CH-, -CH=CH-N=CH-; and,

the carbon atom designated * constitutes a center of chirality; and

(b) an acid addition salt of any one of said compounds having the formula (I) which contains a nitrogen atom susceptible of protonation.

4. A method of treating a cancerous condition in a mammal which comprises administering thereto an effective amount of a substantially chirally pure (R)-compound, a substantially chirally pure (S)-compound, or a mixture of (R)- and (S)-compounds selected from the group consisting of

(a) compounds having the formula (I):



I.

wherein:

each of R^1 and R^2, independently of the other, is selected from the group consisting of alkyl of 1 to 4 carbon atoms, alkoxy of 1 to 4 carbon atoms, cyano, cycloalkoxy of 3 to 18 carbon atoms, cycloalkyl of 3 to 18 carbon atoms, and cycloalkylmethoxy in which cycloalkyl has from 3 to 18 carbon atoms;

one of X and X' is =C=O and the other of X and X' is =C=O or $=CH_2$;

R^3 is selected from $-SO_2$-Y, -COZ, -CN, and hydroxyalkyl of 1 to 6 carbon atoms in which

Y is selected from alkyl of 1 to 6 carbon atoms, phenyl, and benzyl;

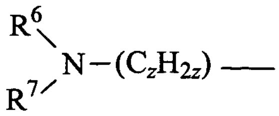
Z is selected from $-NR^{6''}R^{7''}$, alkyl of 1 to 6 carbon atoms, phenyl, and benzyl;

$R^{6''}$ is selected from hydrogen, alkyl of 1 to 4 carbon atoms, cycloalkyl of 3 to 18 carbon atoms; phenyl, benzyl, and alkanoyl of 2 to 5 carbon atoms, each of which is unsubstituted or substituted with halo, amino, or alkylamino of 1 to 4 carbon atoms;

$R^{7''}$ is alkyl of 1 to 4 carbon atoms;

n has a value of 1, 2, or 3;

one of R^4 and R^5 is hydrogen and the other of R^4 and R^5 is, imidazolyl, pyrrolyl, oxadiazolyl, triazolyl, or



$$R^6R^7N-(C_zH_{2z})-$$

in which *z* is 0 or 1;

R^6 when taken independently of R^7, is selected from cycloalkanoyl of 2 to 6 carbon atoms each of which is unsubstituted or substituted with halo, amino, monoalkylamino or dialkylamino in which each alkyl group contains 1 to 4 carbon atoms; and

R^7 is selected from hydrogen, alkyl of 1 to 4 carbon atoms, methylsufonyl, and alkoxyalkylcarbonyl of 2 to 5 carbon atoms; or,

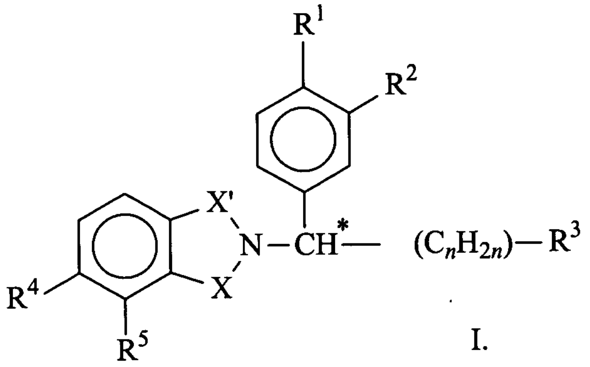
R^6 and R^7 taken together are alkylidene of 1 or 2 carbon atoms substituted by amino, alkylamino, or dialkylamino in which each alkyl group has from 1 to 4 carbon atoms or, provided z is 1, -CH=CH-CH=CH-, -CH=CH-N=CH-; and,

the carbon atom designated * constitutes a center of chirality; and

(b) an acid addition salt of any one of said compounds having the formula (I) which contains a nitrogen atom susceptible of protonation.

5. A method of treating an inflammatory disease or an autoimmune disease in a mammal which comprises administering thereto an effective amount of a substantially chirally pure (R)-compound, a substantially chirally pure (S)-compound, or a mixture of (R)- and (S)- compounds selected from the group consisting of

(a) compounds having the formula (I):



I.

wherein:

each of R^1 and R^2, independently of the other, is selected from the group consisting of alkyl of 1 to 4 carbon atoms, alkoxy of 1 to 4 carbon atoms, cyano, cycloalkoxy of 3 to 18 carbon atoms, cycloalkyl of 3 to 18 carbon atoms, and cycloalkylmethoxy in which cycloalkyl has from 3 to 18 carbon atoms;

one of X and X' is =C=O and the other of X and X' is =C=O or $=CH_2$;

R^3 is selected from $-SO_2-Y$, -COZ, -CN, and hydroxyalkyl of 1 to 6 carbon atoms in which

Y is selected from alkyl of 1 to 6 carbon atoms, phenyl, and benzyl;

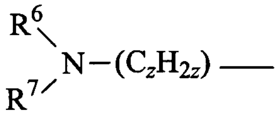
Z is selected from $-NR^{6''}R^{7''}$, alkyl of 1 to 6 carbon atoms, phenyl, and benzyl;

$R^{6''}$ is selected from hydrogen, alkyl of 1 to 4 carbon atoms, cycloalkyl of 3 to 18 carbon atoms; phenyl, benzyl, and alkanoyl of 2 to 5 carbon atoms, each of which is unsubstituted or substituted with halo, amino, or alkylamino of 1 to 4 carbon atoms;

$R^{7''}$ is alkyl of 1 to 4 carbon atoms;

n has a value of 1, 2, or 3;

one of R^4 and R^5 is hydrogen and the other of R^4 and R^5 is, imidazolyl, pyrrolyl, oxadiazolyl, triazolyl, or



$$R^6R^7N-(C_zH_{2z})-$$

in which *z* is 0 or 1;

R^6 when taken independently of R^7, is selected from cycloalkanoyl of 2 to 6 carbon atoms each of which is unsubstituted or substituted with halo, amino, monoalkylamino or dialkylamino in which each alkyl group contains 1 to 4 carbon atoms; and

R^7 is selected from hydrogen, alkyl of 1 to 4 carbon atoms, methylsufonyl, and alkoxyalkylcarbonyl of 2 to 5 carbon atoms; or,

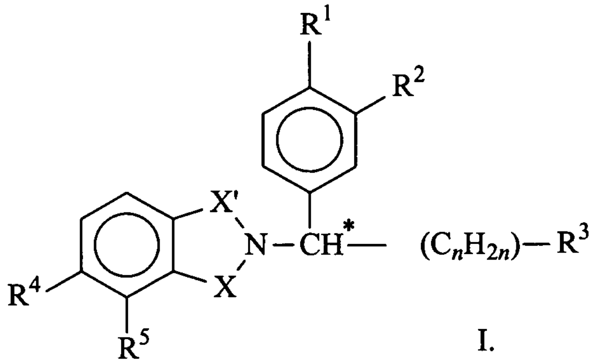
R^6 and R^7 taken together are alkylidene of 1 or 2 carbon atoms substituted by amino, alkylamino, or dialkylamino in which each alkyl group has from 1 to 4 carbon atoms or, provided z is 1, -CH=CH-CH=CH-, -CH=CH-N=CH-; and,

the carbon atom designated * constitutes a center of chirality; and

(b) an acid addition salt of any one of said compounds having the formula (I) which contains a nitrogen atom susceptible of protonation.

6. A method of treating one or more conditions selected from the group consisting of septic shock, sepsis, endotoxic shock, hemodynamic shock and sepsis syndrome, post ischemic reperfusion injury, malaria, mycobacterial infection, meningitis, psoriasis, congestive heart failure, fibrotic disease, cachexia, graft rejection, cancer, autoimmune disease, opportunistic infections in AIDS, rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis, other arthritic conditions, Crohn's disease, ulcerative colitis, multiple sclerosis, systemic lupus erythrematosis, ENL in leprosy, radiation damage, asthma, and hyperoxic alveolar injury in a mammal which comprises administering thereto an effective amount of a substantially chirally pure (R)-compound, a substantially chirally pure (S)-compound, or a mixture of (R)- and (S)- compounds selected from the group consisting of

(a) compounds having the formula (I):



I.

wherein:

each of R^1 and R^2, independently of the other, is selected from the group consisting of alkyl of 1 to 4 carbon atoms, alkoxy of 1 to 4 carbon atoms, cyano, cycloalkoxy of 3 to 18 carbon atoms, cycloalkyl of 3 to 18 carbon atoms, and cycloalkylmethoxy in which cycloalkyl has from 3 to 18 carbon atoms;

one of X and X' is =C=O and the other of X and X' is =C=O or $=CH_2$;

R^3 is selected from $-SO_2-Y$, -COZ, -CN, and hydroxyalkyl of 1 to 6 carbon atoms in which

Y is selected from alkyl of 1 to 6 carbon atoms, phenyl, and benzyl;

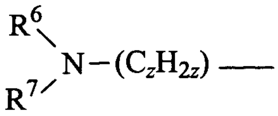
Z is selected from $-NR^{6''}R^{7''}$, alkyl of 1 to 6 carbon atoms, phenyl, and benzyl;

$R^{6''}$ is selected from hydrogen, alkyl of 1 to 4 carbon atoms, cycloalkyl of 3 to 18 carbon atoms; phenyl, benzyl, and alkanoyl of 2 to 5 carbon atoms, each of which is unsubstituted or substituted with halo, amino, or alkylamino of 1 to 4 carbon atoms;

$R^{7''}$ is alkyl of 1 to 4 carbon atoms;

n has a value of 1, 2, or 3;

one of R^4 and R^5 is hydrogen and the other of R^4 and R^5 is, imidazolyl, pyrrolyl, oxadiazolyl, triazolyl, or



$$R^6R^7N-(C_zH_{2z})-$$

in which *z* is 0 or 1;

R^6 when taken independently of R^7, is selected from cycloalkanoyl of 2 to 6 carbon atoms each of which is unsubstituted or substituted with halo, amino, monoalkylamino or dialkylamino in which each alkyl group contains 1 to 4 carbon atoms; and

R^7 is selected from hydrogen, alkyl of 1 to 4 carbon atoms, methylsufonyl, and alkoxyalkylcarbonyl of 2 to 5 carbon atoms; or,

R^6 and R^7 taken together are alkylidene of 1 or 2 carbon atoms substituted by amino, alkylamino, or dialkylamino in which each alkyl group has from 1 to 4 carbon atoms or, provided z is 1, -CH=CH-CH=CH-, -CH=CH-N=CH-; and,

the carbon atom designated * constitutes a center of chirality; and

(b) an acid addition salt of any one of said compounds having the formula (I) which contains a nitrogen atom susceptible of protonation.